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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,026	01/11/2002	Jean-Luc Ridet	A3400PCT-US	5435

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ROSS J. OEHLER
AVENTIS PHARMACEUTICALS INC.
ROUTE 202-206
MAIL CODE: D303A
BRIDGEWATER, NJ 08807

EXAMINER	
NICHOLS, CHRISTOPHER J	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 06/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/868,026	RIDET ET AL.	
	Examiner	Art Unit	
	Christopher Nichols, Ph.D.	1647	

-- Th MAILING DATE of this communication appears on the cov r sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *14-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election **with** traverse of Group I (claims **1-13**) drawn to a method of producing an essentially pure population of astrocytes and the essentially pure population of astrocytes made by said method in Paper No. 8 (17 April 2003) is acknowledged. The traversal is on the ground(s) that Wu and Schwartz (15 March 1998) "Cell Culture Models for Reactive Gliosis: New Perspectives." Journal of Neuroscience Research **51**(6): 675-681 does not disclose a method of producing an essentially pure population of astrocytes. This is not found persuasive because Wu and Schwartz disclose several methodologies of producing essentially pure astrocyte cultures in vitro (see "TISSUE CUTLURE MODELS FOR STUDYING REACTIVE ASTROCYTES"; pp. 676-678). Claims **14-32** are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8 (17 April 2003). The requirement is still deemed proper and is therefore made FINAL.

Status of Application, Amendments, and/or Claims

2. Claims 1-13 are under examination and claims 14-32 are withdrawn from consideration.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims **1, 2, 3, 4, 5, 6,** and **13** are rejected under 35 U.S.C. 102(b) as being anticipated by De Groot *et al.* (1997) "Establishment of Human Adult Astrocyte Cultures Derived from Postmortem Multiple Sclerosis and Control Brain and Spinal Cord Regions: Immunophenotypical and Functional Characterization" Journal of Neuroscience Research **49**: 342-354 (**IDS #BU**). De Groot *et al.* (1997) teaches a method of isolating an essentially pure culture of astrocytes from "resected tissue samples from brain or spinal cord" of adult humans which were grown as an adherent culture in 80 cm^2 flasks that were incubated for 48 hours at which time the "culture medium was changed to remove unattached cells and myelin debris" thus meeting the limitations of claims 1, 2, 3, 5, 6, and 13 ("**Astrocyte-Enriched Cell Cultures**" pp. 344). De Groot *et al.* (1997) also teaches that said method yielded a cell culture comprising 98% $GFAP^+$ astrocytes and no microglia thus meeting the limitations of claims 4 and 13 (pp. 347).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims **7-12** are rejected under 35 U.S.C. 103(a) as being unpatentable over De Groot *et al.* (1997) "Establishment of Human Adult Astrocyte Cultures Derived from Postmortem Multiple Sclerosis and Control Brain and Spinal Cord Regions: Immunophenotypical and Functional Characterization" Journal of Neuroscience Research **49**: 342-354 (IDS #BU) in view of US 5627047 (6 May 1997) Brenner *et al.* and US 5202120 (13 April 1993) Silver *et al.*

5. De Groot *et al.* (1997) "Establishment of Human Adult Astrocyte Cultures Derived from Postmortem Multiple Sclerosis and Control Brain and Spinal Cord Regions: Immunophenotypical and Functional Characterization" Journal of Neuroscience Research **49**: 342-354 (IDS #BU). De Groot *et al.* (1997) teaches a method of isolating an essentially pure culture of astrocytes from "resected tissue samples from brain or spinal cord" of adult humans which were grown in 802 cm flasks that were incubated for 48 hours at which time the "culture medium was changed to remove unattached cells and myelin debris" thus meeting the limitations of claims 1, 2, 3, 5, 6, and 13 ("**Astrocyte-Enriched Cell Cultures**" pp. 344). De Groot *et al.* (1997) also teaches that said method yielded a cell culture comprising 98% $GFAP^+$ astrocytes and no microglia thus meeting the limitations of claims 4 and 13 (pp. 347). De Groot *et al.* (1997) does not teach the transformation of said astrocytes with heterologous nucleic acids.

6. US 5627047 teaches the transformation of astrocytes with heterologous nucleic acids encoding hormones, growth factors, and their receptors using the calcium phosphate method thus meeting the limitations of claims 7 and 12 (Col. 3 lines 25-30; Col. 5 line 40; Col. 9 lines 10-27; Col. 10 lines 40-65; Table 1).

7. US 5202120 teaches that astrocytes may be immortalized by procedures known in the art, so as to preserve sources of such astrocytes for future use. Immortalized astrocytes can be maintained in vitro indefinitely. Various method of immortalization are known in the art and can be used including but not limited to viral transformation (e.g. SV40, polyoma, RNA or DNA tumor viruses, Epstein Barr Virus, bovine papilloma virus), chemical mutagenesis. The viral vectors are usually replication defective the meeting the limitations of claims 8-10 (Col. 13 lines 40-60).

8. It would be obvious to a person of ordinary still in the time of the invention to combine the astrocyte cell line as taught by De Groot *et al.* (1997) with the heterologous nucleic acids as taught by US 5627047 using the viral vectors taught by US 5202120 because the immortalized astrocyte cell lines are useful for research and therapy purposes and when immortalized can be maintained indefinitely (US 5627047 Col. 1 lines 25-55 and US 5202120 Col. 13 lines 40-60).

9. A person of ordinary skill in the art at the time of the invention would be motivated to make an astrocyte cell line using the methods taught by US 5627047 because US 5627047 that astrocytes perform a variety of structural and metabolic functions and thus are central to understanding brain function (Col. 1 lines 25-55).

10. A person of ordinary still in the at the time of the invention would have a reasonable expectation of success because US 5627047 clearly demonstrates the transfection of astrocytes with heterologous nucleic acids (claims 1-37).

11. Thus the invention as a whole was *prima facia* obvious over the prior art.

Summary

12. Claims **1-13** are hereby rejected.

13. It is of note that numerous transfection methods are known in the art and can be used to make the claimed astrocyte cell line such as viral vectors such as retrovirus, modified herpes viral vectors, herpes-viral, adenovirus, adeno-associated virus) or by direct DNA transfection (lipofection, calcium phosphate transfection, DEAE-dextran, electroporation) [US 5750376 (12 May 1998) Weiss *et al.*]

14. It is of note that the IDS is replete with references describing the use of replication defective viral vectors to transform astrocytes including but not limited to:

a. Castillo *et al.* (1994) "Retinal ganglion cell survival is promoted by genetically modified astrocytes designed to secrete brain-derived neurotrophic factor (BDNF)." Brain Research **647**: 30-36 (**IDS # AG**)

b. Cunningham *et al.* (1994) "Nerve growth factor released by transgenic astrocytes enhances the function of adrenal chromaffin cell grafts in a rat model of Parkinson's disease." Brain Research **658**: 219-231 (**IDS # AI**)

c. Cunningham *et al.* (1991) "The use of genetically altered astrocytes to provide nerve growth factor to adrenal chromaffin cells grafted into the striatum." Brain Research **561**: 192-202 (**IDS # AJ**)

d. Lin *et al.* (10 February 1997) "Human Fetal Astrocytes as an *Ex Vivo* Gene Therapy Vehicle for Delivering Biologically Active Nerve Growth Factor." Human Gene Therapy **8**: 331-339 (**IDS # BA**)

e. Yoshimoto *et al.* (1995) "Astrocytes retrovirally transduced with BDNF elicit behavioral improvement in a rat model of Parkinson's disease." Brain Research **691**: 25-36 (**IDS # BT**)

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is 703-305-3955. The examiner can normally be reached on Monday through Friday, 8:00AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Gary Kunz, Ph.D.** can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications. The fax phone numbers for the customer service center is 703-872-9305

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Elizabeth C. Kemmerer

CJN
June 21, 2003

ELIZABETH KEMMERER
PRIMARY EXAMINER